Occurrence and Fate of Pharmaceuticals and Antiseptics in Drinking and Surface Waters

Project Scope

Although several European studies have revealed a number of pharmaceuticals present in surface waters, sewage treatment plant effluents, and drinking water, information concerning the occurrence, fate, and ecological risk of selected pharmaceuticals and antiseptics in the United States is extremely limited. The research conducted under this grant is designed to address these data gaps by providing an assessment of the prevalence of common pharmaceuticals in drinking water, sewage treatment plant influents and effluents, and receiving waters in the United States.

The specific goals of the research conducted under this grant were to:

1. Compile data on pharmaceutical usage, expected introductory concentrations, and potential environmental risks and select target compounds for detailed evaluation.
2. Refine analytical methods for the quantification of selected pharmaceuticals in sewage and drinking water samples. The methods under investigation involve the use of standard gas chromatography/mass spectrometry (GC/MS) techniques that can be adopted readily for use at other laboratories.
3. Examine the biodegradability of selected compounds in simulated wastewater treatment systems; examine interactions between contaminants and impacts on biodegradability at the low levels encountered in the environment.
4. Extend developed methods to analyze water samples for target pharmaceuticals collected from a number of sources, including raw and finished drinking water from public utilities to relate removal efficiency to

Grant Title and Principal Investigators

Pharmaceuticals and Antiseptics: Occurrence and Fate in Drinking Water, Sewage Treatment Facilities, and Coastal Waters (EPA Grant #R829004)

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Key Findings and Implications

Analytical Accomplishments:

- Compiled recent usage and ecotoxicity data for "high use" pharmaceuticals. Expected introductory concentrations estimated from the usage data were generally within an order of magnitude of measured concentrations in untreated U.S. wastewaters.
- Analytical methods were developed using modified gas chromatography/mass spectrometry (GC/MS) techniques to measure pharmaceuticals and personal care products in water with high reproducibility and at lower detection limits in a cost-effective and time-efficient manner. These methods could be easily extended to other analytes as well.
- The high sensitivity attained in these experiments is sufficient for analyzing trace concentrations in drinking water. The methods employ standard benchtop GC/MS equipment and techniques.
- Biodegradation experiments were carried out on selected pharmaceuticals. The results from these experiments will prove useful in determining the fate of these compounds in the environment and in treatment systems.

Implications of Research:

- Methods developed under this research can be applied to support the evaluation of pharmaceutical occurrence in natural and treated waters.
- Results from this study provide exposure data needed to assess whether human and ecological effects could be associated with pharmaceuticals in environmental water systems.

Publications include 5 articles in preparation for submission in peer-reviewed journals and 9 conference/workshop presentations.

Project Period: September 2001 to August 2005

Relevance to ORD's *Drinking Water Research Multi-Year Plan* (2003 Edition)

This project contributes directly to the second and third Long-term Goals for drinking water research: (2) by 2010, develop new data, innovative tools and improved technologies to support decision making by the Office of Water on the Contaminant Candidate List and other regulatory issues, and implementation of rules by states, local authorities, and water utilities; and (3) By 2009, provide data, tools and technologies to support management decisions by the Office of Water, state, local authorities and utilities to protect source water and the quality of water in the distribution system.

In the United States, there is only limited information concerning the occurrence, fate, and potential ecological risk of pharmaceuticals in environmental waters. The overall objective of this research project is to provide a preliminary assessment of the likely occurrence patterns of widely used pharmaceuticals in drinking water, sewage treatment plant influent and effluent, and receiving waters, and to refine analytical methods for characterizing pharmaceutical occurrence. This information will help EPA and water authorities to determine if pharmaceuticals in the water supply are of concern.

treatment processes; coastal waters obtained from the Upper Chesapeake Bay to examine evidence of rapid natural attenuation; and influent and effluent samples from STPs to examine the adequacy of current wastewater treatment practices.

These experiments were part of an overall research plan to evaluate the occurrence of widely-used pharmaceuticals in environmental waters. Some of the analyses are still ongoing as this grant is still in progress. Thus, some of the results summarized below are preliminary.

Project Results and Implications

Compilation and Evaluation of Pharmaceutical Data: A detailed usage and ecotoxicity database has been constructed for the highest volume ("Top 200") pharmaceuticals in the brand name, generic, over-the-counter, and hospital categories for the years 1999, 2000, and 2002. In addition, other factors that have been used to identify high-priority chemicals include chemical or therapeutic class, likely toxicity (estimated using ECOSAR[1] where measured toxicity data are unavailable), and amenability to GC/MS analysis following derivatization (if required). Because very few of the "Top 200" pharmaceuticals appear in the U.S. Environmental Protection Agency (EPA) ECOTOX (ecotoxicology) database, selection of analytes has relied heavily on the combination of estimated production data obtained by combining sales data and average wholesale price, and estimated toxicity.

When possible, a risk assessment was performed to assess the potential for ecological toxicity of the "high use" pharmaceuticals by comparing expected introductory concentrations (EICs) to measured or predicted toxicity criteria for freshwater organisms. The EICs estimated from the usage data were generally within an order-of-magnitude of measured concentrations in untreated U.S. wastewaters. The results from the risk assessment indicated that several pharmaceuticals (e.g., gemfibrozil, gabapentin) have the potential to be present in the surface waters at ecologically significant levels. The risk assessment results are useful in focusing attention on existing pharmaceuticals that could pose ecological risks. In addition, a number of other potentially ecotoxic pharmaceuticals have been identified through this process, many of which have not been targeted by other investigators.

[1] ECOSAR (ecological structure-activity relationships) is a personal computer program developed and provided by EPA (http://www.epa.gov/oppt/newchems/21ecosar.htm) that can be used to estimate the ecological toxicity of industrial chemicals. The program predicts the toxicity of chemicals to aquatic organisms (e.g., fish, invertebrates, algae) using structure-activity relationships (SARs).

Analytical Method Refinement for Quantification: The investigators developed two new multi-compound derivatization methods for analysis of acidic, neutral, and basic pharmaceuticals and personal-care products employing either pentafluorobenzyl bromide or a combination of *N*, *N*-bis(trimethylsilyl)-trifluoroacetamide and chlorotrimethylsilane. The methods allow for the analysis of 53 pharmaceuticals and personal care products from a split sample, and provide high reproducibility and low detection limits in a cost-effective and time-saving manner. Twenty-four of these 53 analytes do not appear to have been targeted by previous investigations in the United States. The method developed for acidic compounds is particularly robust, and offers substantial benefits over previous pentafluorobenzylation methods, in that it performs best in a water:organic solvent mixture—thus eliminating the need for drying of a solvent extract prior to derivatization or drying of the solid phase extraction (SPE) cartridge. The derivatization method can be applied readily to other laboratory systems in which concentration via SPE is not needed, such as to batch biodegradation experiments, in which the derivatization is conducted prior to a solvent extraction step. The derivatives formed by the pentafluorobenzylation method are quite stable and are not destroyed on contact with traces of water.

A solid phase extraction procedure was also developed and optimized to provide ultra-low detection limits for the compounds of interest. The SPE procedure also proved to be precise, exhibiting little interference when extracting target analytes in water containing high levels of humic acid or natural organic matter. Optimization experiments also confirmed the superiority of recently developed polymeric sorbents over traditional C_{18} cartridges for extracting neutral and acidic drugs from water. These methods have been shown to perform well in highly complex matrices, such as raw and treated wastewater obtained from publicly owned treatment plants, as demonstrated by high recoveries obtained using isotopically labeled surrogate compounds purchased or synthesized in the researchers' laboratory, or laboratory-fortified field matrices for those compounds for which isotopically labeled surrogates could not be synthesized.

Selection of target compounds for water analyses was based in part on calculations of expected introductory concentrations, as well as ongoing screening studies conducted on sewage treatment plant influents. Persistence and environmental risk also were taken into account. The analytical methods described above provided the sensitivity needed to quantify 35 pharmaceuticals and personal care products of the 53 analytes sought in raw or treated wastewater. The high sensitivity attained in these experiments is adequate for analyzing trace pharmaceutical concentrations in drinking water, using standard GC/MS equipment and techniques. This will facilitate future studies of pharmaceuticals as environmental contaminants by other research groups.

Biodegradability of Selected Compounds: The objective of these studies was to understand compound interactions that may occur during biodegradation. Batch biodegradation experiments were conducted with different electron acceptors, microbial inocula, and concentrations to gain insight into the biodegradation behavior of our target analytes. The aerobic batch biodegradation experiments showed that most of the products tested underwent greater than 80 percent biodegradation when initially present at low concentrations. These experiments also have revealed that different microbial communities were capable of degrading different compounds. For anaerobic (nitrate and iron reducing) biodegradation experiments, most of the target analytes exhibited greater than 60 percent biotransformation. Iron reducing conditions revealed biotransformation results similar to that encountered under nitrate reducing conditions. Within the ranges studied, the initial concentration exerted little effect on the extent of aerobic or anaerobic biodegradability. These results will prove useful in determining the fate of these target compounds in the environment and in assessing the potential limitations associated with normal analytical screening methods conducted with defined media. Studies are being conducted to examine the removal of pharmaceuticals in the presence of other compounds in order to determine whether toxic and/or inhibitory effects introduced by interactions with antimicrobials or antiseptic compounds could limit biodegradability in actual wastewater.

Analysis of Pharmaceuticals in Water Samples: Researchers are currently analyzing pharmaceuticals in different waters by extending the methods developed in this research. To examine the efficiency of removal of pharmaceuticals in wastewater by treatment processes, the investigators measured concentrations of target compounds in raw and treated wastewater from publicly owned sewage treatment plants in Baltimore, Maryland, and Yonkers, New York. In addition, samples are currently being collected and analyzed from sewage treatment plants in Philadelphia, Pennsylvania, and Washington, D.C.; arrangements are also being made to secure samples from other urban centers along the East Coast. Efforts have also recently been undertaken to analyze waste streams from hospitals in the greater Baltimore area to determine the relative contribution of these facilities to pharmaceutical loading in municipal sewage treatment plants. Finally, plans are under way to analyze pharmaceuticals in coastal waters (water samples from the Upper Chesapeake Bay) to investigate the natural attenuation of pharmaceuticals in the environment. The low detection limits of the analytical methods described should provide good resolution necessary for interpreting differences in contaminant distributions and assessing dilution from fresh and salt water sources.

Investigators

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For More Information

NCER Project Abstract and Reports:

http://cfpub2.epa.gov/ncer_abstracts/index.cfm/fuseaction/display.abstractDetail/abstract/1061/report/0

Peer Reviewed Publications

None.